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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/978,297	10/17/2001	Oron Yacoby-Zeevi	01/22716	5033

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EXAMINER	
HUTSON, RICHARD G	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 10/16/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/978,297	YACOBY-ZEEVI, ORON	
	Examiner	Art Unit	
	Richard G. Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7-9,11-17,19-37 and 51-84* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7-9,11-17,19-37 and 51-84* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/11/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/20/2006 has been entered.

Applicant's amendment of the specification and claims 1, 7, 13, 21, 26, 31, 51, 56, 61, 68, 73, 78, in the paper of 7/20/2006, is acknowledged. Claims 1-5, 7-9, 11-17, 19-37 and 51-84 are present for examination. Applicants' arguments filed on 7/20/2006, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 51-84 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of improving embryo implantation, the method comprising contacting an embryo with an effective amount of purified

recombinant heparanase having at the amino acid sequence of SEQ ID NO: 1 and inserting the embryo in a receptive uterus, wherein said embryo and uterus are from the same species, does not reasonably provide enablement for any method of improving embryo implantation, the method comprising contacting any embryo with an effective amount of purified recombinant heparanase having a mere 90% homology to SEQ ID NO: 1 and inserting the embryo in any receptive uterus. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

This rejection was stated in the previous office action. In response to the rejection, applicants have amended claims 1, 7, 13, 21, 26, 31, 51, 56, 61, 68, 73, 78 and traverse the rejection as it applies to the newly amended claims.

Applicants continue to traverse the rejection on the basis that the decision of the Board of Patent Appeals and Interferences in *Ex Parte Sun* dictates a finding of enablement in the instant invention.

Applicants acknowledge the previous examiner's statements that "the factors necessary for the determination of the enablement of the instant claims and that of the referred to decision are different, however, applicants assert that nowhere is it stated "How they are different and why this difference makes a difference in finding enablement of the claims in Sun, but not in the instant application."

Applicants further submit that in Sun, claims to 80% homology were found to be enabled, in contrast to 90% homology claimed here. As previously stated, the factors necessary for the determination of the enablement of the instant claims and that of the

referred to board decision are different. For applicants convenience it is pointed out to applicants that the referred to claims from *Ex parte Sun* are drawn to a wee1 'polynucleotide' having at least 80% identity to the entire coding region of SEQ ID NO: 1 and this is a 403 amino acid encoding polynucleotide. The instant claims are drawn to a "method of improving embryo implantation" comprising contacting an embryo with an effective amount of a purified heparanase having at least 90% homology to SEQ ID NO: 1, wherein said heparanase is pure enough to elicit anti-heparanase antibodies. There are considerably more complex enabling issues to consider in the instant application then tin that of the referred to decision. One is the enablement of a polynucleotide versus the enablement of a method of treatment with a polypeptide. It is acknowledged that when making a decision regarding enablement one must consider the Wands factors and that these are different for every individual situation. These differences include: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

While the examiner has not presented an exhaustive list comparing each of the Wands factors for the instant claims and that of Ex parte Sun, applicants have neither pointed out similarities between the two decisions beyond that the each encompasses a percent homology or identity and a protein or polynucleotide. Thus the current claims

remain rejected under a lack of enablement, for the reason previously stated and of record.

The specification does not support the broad scope of the claims which encompass any method of improving embryo implantation, the method comprising contacting an embryo with an effective amount of purified recombinant heparanase having a mere 90% homology to SEQ ID NO: 1 and inserting the embryo in any receptive uterus, because the specification does not establish: (A) regions of the protein structure which may be modified without effecting heparanase and embryo implantation activity; (B) the general tolerance of heparanases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue of a heparanase with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to retain the heparanase activity necessary to practice the claimed methods and the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable, it would require undue experimentation for one skilled in the art to arrive at the majority of those methods of the claimed genus.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including methods of use of those heparanases

having a mere 90% homology to SEQ ID NO: 1. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of those methods having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of those species in which the disclosed methods are successful is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 1-5, 7-9, 11, 12, 13-17, 19, 20, 21-25, 26-30, 31-37 and 51-84 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This rejection based on new matter was stated in the previous office action. In response to the rejection, applicants have amended claims 1, 7, 13, 21, 26, 31, 51, 56, 61, 68, 73, 78 and traverse the rejection as it applies to the newly amended claims.

Applicants have amended the claims such that they no longer require that " wherein said purified recombinant heparanase can elicit anti-heparanase antibodies" but rather they require that " wherein said purified recombinant heparanase is pure enough to elicit anti-heparanase antibodies".

Applicants submit that the specification discloses that "The recombinant protein may be useful in obtaining pure heparanase, which in turn may be useful in eliciting anti-heparanase antibodies, either poly or monoclonal antibodies" (i.e. page 19, lines 5–9). Applicants submit that given this disclosure, the skilled artisan would certainly understand that "the purified recombinant heparanase" recited in the method claims of the subject invention is pure enough to elicit anti-heparanase antibodies, as disclosed in the specification.

Applicant's amendment and traversal is acknowledged and has been carefully considered, however, is not found persuasive on the following basis. It is understood that one skilled artisan would understand that the purified recombinant heparanse is inherently pure enough to elicit anti-heparanase antibodies, however this inherent property of the subject invention is not recognized or acknowledged as applicants seem to be using it, i.e. as a purity limitation. Thus such a "purity limitation" is not supported by the specification at the time of filing and is thus considered new matter.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-5, 7-9, 11, 12, 13-17, 19, 20, 21-25, 26-30, 31-37 and 51-84 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fuks et al., Gough et al., (U.S. Patent No: 5,962,321) and Goshen et al. (Molecular Human Reproduction, Vol 2, No. 9, pp 679-684, 1996, see IDS).

The rejection is stated in the previous office action as it applies to previous claims 1-5, 7-9, 11, 12, 13-17, 19, 20, 21-25, 26-30, 31-37 and 51-84. In response to the rejection, applicants have amended claims 1, 7, 13, 21, 26, 31, 51, 56, 61, 68, 73, 78 and traverse the rejection as it applies to the newly amended claims.

The original rejection stated that Fuks et al. teach the purification of heparanase obtained from human SK-HEP-1 cells, and it is recognized that the heparanase taught by Fuks et al. inherently has the amino acid sequence of SEQ ID NO: 1.

Applicants continue to submit that the combination of all references is not obvious and is at best an invitation to try, however, to promote the prosecution of the subject application applicants have amended the claims to require that the claimed heparanase be pure enough to elicit anti-heparanase antibodies and further submit a declaration discussing this and thus submit that the rejection be withdrawn.

Applicants amendment that the required heparanase no longer "can elicit anti-heparanase antibodies", but rather the required heparanase "is pure enough to elicit anti-heparanase antibodies" is acknowledged.

Applicant's complete argument is acknowledged and has been carefully considered, however, continues to be found non-persuasive on the following basis.

As previously stated, the preparation taught by Fuks et al. is that of an isolated heparanase, from the same source as applicants claimed heparanase and thus Fuks et al. continues to make obvious applicants claimed isolated heparanase protein for all of the reasons of record. Applicants comments that applicants are not (merely) claiming "an isolated heparanase" but rather a heparanase protein "that is pure enough to elicit anti-heparanase antibodies" is acknowledged and it continues to be the position of the office that the "heparanase" protein taught by Fuks et al. "is pure enough to elicit anti-heparanase antibodies" even if the heparanase protein taught by Fuks et al. was in a composition that "did not elicit anti-heparanase antibodies". The limitation/characteristic that the heparanase of the claimed invention "is pure enough to elicit anti-heparanase antibodies" is an inherent limitation/characteristic of the isolated heparanase taught by Fuks et al.

Thus claims 1-5, 7-9, 11, 12, 13-17, 19, 20, 21-25, 26-30, 31-37 and 51-84 remain obvious over Fuks et al., Gough et al. and Goshen et al.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G. Hutson whose telephone number is (571) 272-0930. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (571) 272-0928. The fax

phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Richard G Hutson, Ph.D.
Primary Examiner
Art Unit 1652

rgh
9/21/2006